Current Methods in Arterial Spin Labeling

In the past few years, ASL has developed into a powerful tool for the measurement of CBF using MRI. In this technique, radiofrequency pulses are used to modify the longitudinal magnetization of arterial blood, generating an endogenous tag or tracer that decays away with a time constant given by the T_1 relaxation time. After a delay to allow for tagged blood to flow into the brain, an MRI image of the brain is acquired that reflects the inflow of tagged blood as well as static brain tissue in the slice. A second (control) image is then acquired in the absence of a preceding tag pulse. The difference between these two images reflects the amount of tagged blood that has been delivered to the imaging region. Under ideal circumstances, this difference signal is itself directly proportional to CBF, but in practice, several additional factors must be considered in order to quantify CBF, including the dynamics of blood delivery, T_1 relaxation of the tag, and intravascular artifacts, among others. These effects have been studied in several laboratories over the past few years, resulting in greatly improved CBF quantitation.

ASL methods can be categorized into pulsed ASL (PASL) (1-6) in which the tagging is applied as a spatially selective pulse, continuous ASL (CASL) (7-9) in which tagging occurs as a flow driven adiabatic inversion through a tagging plane, and velocity selective ASL (VSASL) (10-12) in which the tag is selective for flow velocity. In addition, vessel selective (13-15) and vessel encoded (16) methods are now available to provide quantitative maps of vascular territories of specific vessels. Four classes of applications for ASL are described here, along with appropriate forms of ASL for each.

ASL for Quantitative CBF in Cerebrovascular Disease

In cerebrovascular diseases such as stroke, slow and/or collateral flow conditions can occur, which presents a problem for PASL and CASL methods. In disease states, the transit delay for the delivery of tagged blood from the tagging region to the imaging region can be several times the T_1 of the tagged blood, leading to a reduced or absent ASL signal. VSASL was designed specifically to address this problem, and is in principle insensitive to slow or collateral flow conditions. In VSASL, a velocity selective tag is applied which modulates the longitudinal magnetization of blood flowing above a cutoff velocity V_c. This tag can be applied without any spatial selectivity at all, allowing for the application of a tag that covers all arteries, including circuitous collateral routes of flow. After a delay period TI during which the tagged blood flows down the arterial tree, an image (the tag image) is acquired of all spins whose velocities are below V_c. By imposing the restriction $V < V_c$ for the image acquisition by means of additional velocity selective pulses, the resulting image includes tagged magnetization only from spins that decelerated during TI from above to below V_c. If the velocities in the arterial tree are monotonically decreasing, then

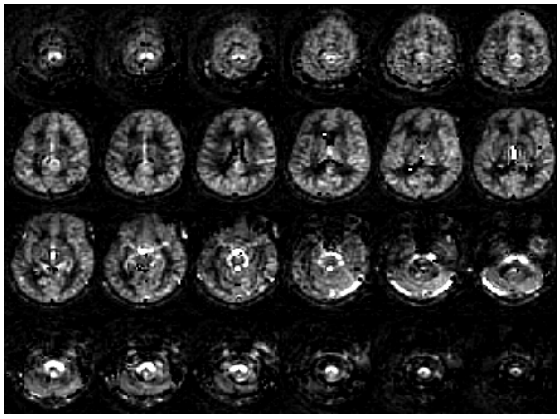

Figure 1: 3D spiral FSE VSASL image. Parameters include: *24cm FOV with 64^2 resolution in-plane; 32-8mm slices; 16 echos; 8 spiral interleaves; V_c=2cm/s; background suppression; scan time 3:12*

the amount of tagged blood that appears in the image is simply TI·CBF, where CBF is the local cerebral blood flow. A second function of the velocity selectivity in the image acquisition is to act as a filter for arterial versus venous blood. In general, venous blood accelerates, and while a large volume of venous blood with $V > V_c$ will be tagged, it will generally still be at $V > V_c$ at the time of image acquisition and will not be detected. Without velocity selectivity in the image acquisition, the VSASL signal would have a potentially large blood volume component, as opposed to being proportional to CBF. An example of a 3D VSASL data set is shown in Figure 1. While this method allows in principle for quantitative CBF imaging in cerebrovascular disease, the insensitivity to slow and collateral flow comes at the cost of decreased SNR (12).

ASL for Quantitative CBF under Normal or High Flow Conditions

For many research and clinical applications there is no reason to expect slow or collateral flow conditions, and more SNR efficient ASL methods can be used. These applications include clinical conditions such as Alzheimer's Disease, Schizophrenia, and fMRI mapping of brain function (17). Under these conditions, CASL methods have the highest SNR efficiency (18). In these techniques, arterial blood is tagged by flow driven adiabatic inversion as it passes through a defined tagging plane. Constant RF and gradient waveforms are used to implement this inversion, and a large amount of tagged magnetization can be delivered in this manner. Recently, a modification of the CASL method, referred to as pseudo-continuous ASL (PCASL) (19), has been introduced in which the continuous RF irradiation is replaced by a series of discrete RF pulses of the same total duration and mean RF amplitude. The continuous gradient is also replaced by a series of discrete gradient pulses with the same mean gradient. PCASL has two distinct advantages over CASL. First, the RF pulses are applied with a much larger resonance offset relative to the spins in the region of interest (ROI). This greatly reduces the contamination of the spins in the ROI by magnetization transfer (MT) effects, which can reduce the signal by 20% or more in conventional CASL. Second, the application of a series of discrete RF pulses is easier to implement on most MR scanner hardware, making the method more portable across scanners. An example of a PCASL image set is shown in Figure 2.

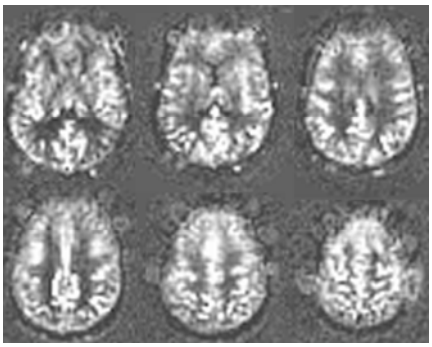

Figure 2: 2D PCASL. Parameters include: *24cm FOV with 64^2 resolution in-plane; 7mm slices; 800ms tag time with 1200ms post labeling delay.*

ASL for Simultaneous CBF and BOLD fMRI

For functional brain imaging, the combination of BOLD and CBF data provides a unique opportunity to measure oxygen metabolism ($CMRO_2$) through calibrated BOLD experiments (20). Combined CBF and BOLD experiments can be efficiently performed using ASL with dual echo acquisitions, the first with minimal BOLD weighting used to calculate the ASL signal, and the second at a longer TE to acquire a BOLD signal. For this application, the choice of ASL tagging methods affects the contamination of the BOLD signal by blood flow, and the contamination of the ASL signal by BOLD contrast (21). A useful feature of PASL is that it can be used with an appropriate combination of tagging and presaturation pulses so that the ASL signal is a simple subtraction between

tag-control pairs, while the BOLD signal is a simple average of tag-control pairs, with minimal contamination between the two (5,21).

ASL for Mapping of Vascular Territories

In the past few years, several ASL methods have been introduced that allow for the imaging of specific perfusion territories. These new methods have several potential clinical applications. For example, in patients with cerebrovascular disease, there are often two or more stenotic vessels, and measurements of the distribution of flow delivered by different arterial supplies can aid in the planning and staging of interventions such as carotid endarterectomy, stenting, or bypass. In patients who will undergo temporary carotid occlusion (ie for tumor or aneurism surgery), prior knowledge of the presence and patterns of collateral circulation could be crucial in assessing the risks of the procedure. When assessing cerebrovascular reserve, having vessel specific CBF maps, and observing shifts in perfusion patterns with pharmacological stress could help to identify which vessels are most likely to become symptomatic. In the evaluation of tumors or arteriovenous malformations (AVMs), mapping of the vascular supplies to the lesion could help in planning interventions such as surgery, embolization or sclerotherapy. In vascular territory imaging (VTI) (13-15), individual or groups of feeding arteries are tagged, and ASL images are acquired that reflect the vascular distribution of those feeding arteries. This can be performed sequentially for each vascular territory of interest. More recently, a vessel encoded method has been introduced that allows for the simultaneous separation of vascular sources in a single acquisition, in principle with the same SNR in the same time as VTI of a single vascular source (16). Thus, for mapping of the territories supplied by left vs right carotid arteries, the vessel encoded method can provide the same information as VTI in half the time, with the same SNR, which can be of great benefit, particularly in an acute setting. For an example of vessel encoded ASL, see abstract entitled “Vessel Encoded Arterial Spin Labeling using Pseudo-Continuous Tagging” at this meeting.

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